start site of the PSA gene was identified. It has been hypothesized that the AR binds the two PSA alleles (A and G) with differing affinity and hence may differently influence prostate cancer risk. We have investigated the potential functional significance of this polymorphism and its association with prostate cancer susceptibility in 145 men diagnosed with prostate cancer and 219 healthy men. PSA polymorphism was determined by the PCR-restriction fragment length polymorphism analysis using DNA from peripheral blood samples. We did not find a significant association between PSA polymorphism at position –158 and prostate cancer risk. The OR, calculated relative to subjects with the A/A genotype, was for the A/G genotype 0.95 (95% CI 0.56–1.6), and for the G/G genotype 0.62 (95% CI 0.34–1.12), respectively. No significant associations were found between the PSA polymorphism and the serum PSA level ($P = 0.49$). In conclusion, the PSA-158 ARE-I genetic polymorphism may not be associated with the risk of prostate cancer development and its disease progression.

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Study of drug resistance in patients with acute leukaemia: determination of mRNA ABC-transporters and apoptotic proteins

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Cellular drug resistance is an important determinant of the response to chemotherapy, and its precise measurement may have clinical relevance. Various cellular mechanisms can give rise to multidrug resistance (MDR). Expression of ATP binding cassette (ABC) transporters and apoptotic proteins is the best-studied mechanism of chemoresistance. In presented study, expression of several ABC efflux pumps (P-gp, MRP, BCRP) and apoptotic proteins (p53, bax, bcl-2 and bcl-x) have been studied by RT-PCR in leukaemic cells of patients with acute leukaemia. In addition, our study focuses on determination levels of mRNA apoptotic proteins among leukaemic cells and normal lymphocytes from healthy donors. We have demonstrated that acute leukaemia, both myeloblastic (AML) and lymphoblastic (ALL), is associated with significantly elevated levels of p53 and bax mRNA in leukaemic cells. With respect to ALL, significantly elevated levels of bcl-xl mRNA could explain for relative resistance of ALL cells to p53-dependent apoptosis. P-gp exhibited strong variation in transcription level among different leukaemia patients; however, it was significantly higher in relapsed than in de novo patients. The expression of MRP was more consistent and no significant differences between de novo and relapsed patients were observed. The expression level of BRCP was very low, however, significantly higher in relapsed than in de novo patients. Supported by grant aAV/1106/2004 from Ministry of Education of Slovak Republic.

Late abstracts

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Chemoprevention of kava and its potential active components against lung tumorigenesis in A/J mouse induced by 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone and benzo(a)pyrene

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Lung cancer has been the leading cause of death among all the malignancies for decades with relatively small improvement in its treatment. Preventing the development of lung cancer, therefore, would be an alternative strategy to help fight this disease. As smoking is the major cause of lung cancer, smokers and ex-smokers would be the population to benefit the most from an effective lung chemopreventive agent.

Based on epidemiological information, kava – a traditional beverage in the South Pacific Island region, is potentially chemopreventive against lung tumorigenesis. Its chemopreventive effect, however, has never been evaluated. In addition, the potential hepatotoxicity of kava presents a major barrier to its chemopreventive application. In this study, we evaluated whether oral kava could prevent NNK- and B[a]P-induced lung tumorigenesis in A/J mouse and whether such kava treatment would induce hepatotoxicity.

Lung tumorigenesis was induced in A/J mouse with weekly gavage administration of 2 μmol NNK and 2 μmol B[a]P for eight consecutive weeks. To evaluate the potential chemopreventive activity, kava was administered orally as a supplement to standard diet at the dose of 10 mg/g diet. Such diet was administered to A/J mice (20 mice per group) through three courses – either administered only during the carcinogen-treatment (eight weeks); or administration started after the last carcinogen treatment (22 weeks); or administered throughout the whole experimental period (30 weeks). It was found that the 30-week kava treatment had statistically significant lower lung tumor multiplicities (i.e., mean number of tumors/mouse) than NNK + B[a]P-treated mice [12.8 tumors/mouse in the NNK + B[a]P group versus 5.65 tumors/mouse in the NNK + B[a]P + Kava group; difference, 7.15 tumors/mouse; 95% CI, 3.9 to 10.6 tumors/mouse; $P < 0.0001$], corresponding to a 55.9% of tumor reduction. The 8-week treatment concurrent with carcinogen treatment also significantly reduced lung tumor multiplicities [12.8 tumors/mouse in the NNK + B[a]P group versus 6.79 tumors/mouse in the NNK + B[a]P + Kava group; difference, 6.01 tumors/mouse; 95% CI, 2.4 to 9.7 tumors/mouse; $P = 0.0018$], corresponding to a 47.1% of tumor reduction. More excitingly, post-carcinogen treatment reduced the tumor multiplicity significantly as well [12.8 tumors/mouse in the NNK + B[a]P group versus 6.59 tumors/mouse in the NNK + B[a]P + Kava group; difference, 6.21 tumors/mouse; 95% CI, 2.6 to 9.9 tumors/mouse; $P = 0.0014$], corresponding to a 48.7% of tumor reduction. Mechanistically, kava inhibited proliferation and enhanced apoptosis of lung cancer cells as demonstrated by a reduction of proliferating cell nuclear antigen (PCNA), an increase of caspase-3 and cleavage of Poly (ADP-ribose) polymerase (PARP). Kava treatment inhibited the activation of nuclear factor-κB (NF-κB), a potential up-stream pathway of kava chemoprevention. Under these treatments, kava induced no detectable hepatotoxicity as characterized by the following parameters – body weight, liver weight, ALT, AST, GGT enzymatic activities, and liver pathology. In this